

## **REMARKS/ARGUMENTS**

The foregoing amendments in the specification and claims are of formal nature, and do not add new matter.

Prior to the present amendment, Claims 28-33 were pending in this application and were rejected on various grounds. Claim 33 has been cancelled without prejudice. The rejection of the remaining claims is respectfully traversed.

### **Specification**

The specification has been amended to remove embedded hyperlink and/or other form of browser-executable code.

### **Priority**

The Examiner had stated that Applicants were entitled to the priority of U.S. Application No. 09/946,374, filed 9/4/01 based on chondrocyte re-differentiation assay (Example 150, Assay 110). Applicants respectfully submit that the chondrocyte re-differentiation assay for support of patentable utility was first disclosed in International Application No. PCT/US00/04342, filed on February 18, 2000, the priority of which is claimed in the present application. Accordingly, the present application is entitled to at least the February 18, 2000 priority. Page 523 of the PCT publication, WO 00/78961, corresponding to PCT application, PCT/US00/04342, is enclosed herewith.

### **Claim Rejections – 35 U.S.C. §112, Second Paragraph**

Claims 33 is rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner noted that "[t]he term 'specifically' ... is a relative term which renders the claims indefinite." Applicants respectfully disagree.

Without acquiescing to the Examiner's position in the current rejection and solely in the interest of expedited prosecution in this case, Claim 33 has been canceled and Claim 28 has been amended to recite "specifically binds". Applicants submit that the art-recognized meaning of "specific" binding is that the antibody that specifically binds to a particular antigen does not significantly cross-react with another antigen. Therefore, the term "specifically binds" in

Claim 28 clearly refers to an antibody that is able to bind to the polypeptide of SEQ ID NO:116 without significantly cross reacting with another antigen. Accordingly, one skilled in the art would clearly know what the scope of the invention is, and the present rejection should be withdrawn.

**Claim Rejections – 35 U.S.C. §102**

Claims 28-33 are rejected under 35 U.S.C. §102(a) as being allegedly anticipated by Baker *et al.*, WO 00/12708 (publication date March 9, 2000). As discussed above, Applicants are entitled to an effective filing date of February 8, 2000. Accordingly, Baker *et al.* is not prior art under 102(a) since its publication date is after the effective priority date of the present application. Hence, Applicants respectfully request that this rejection be withdrawn.

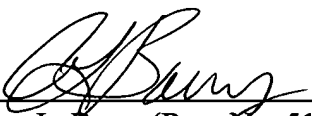
Claims 28-33 are rejected under 35 U.S.C. §102(a) as being allegedly anticipated by Yang *et al.*, WO 01/51638 (publication date July 19, 2001). As discussed above, Applicants are entitled to an effective filing date of February 8, 2000. Accordingly, Yang *et al.* is not prior art under 102(a) since its publication date is after the effective priority date of the present application. Hence, Applicants respectfully request that this rejection be withdrawn.

All claims pending in the present application are believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. **08-1641** (Attorney's Docket No. **39780-2830 P1C6**). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: June 8, 2004

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**EXAMPLE 149: Detection of PRO Polypeptides That Affect Glucose or FFA Uptake by Primary Rat Adipocytes (Assay 94)**

This assay is designed to determine whether PRO polypeptides show the ability to affect glucose or FFA uptake by adipocyte cells. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of disorders where either the stimulation or inhibition of glucose uptake by adipocytes would be beneficial including, for example, obesity, diabetes or hyper- or hypo-insulinemia.

In a 96 well format, PRO polypeptides to be assayed are added to primary rat adipocytes, and allowed to incubate overnight. Samples are taken at 4 and 16 hours and assayed for glycerol, glucose and FFA uptake. After the 16 hour incubation, insulin is added to the media and allowed to incubate for 4 hours. At this time, a sample is taken and glycerol, glucose and FFA uptake is measured. Media containing insulin without the PRO polypeptide is used as a positive reference control. As the PRO polypeptide being tested may either stimulate or inhibit glucose and FFA uptake, results are scored as positive in the assay if greater than 1.5 times or less than 0.5 times the insulin control.

The following PRO polypeptides tested positive as stimulators of glucose and/or FFA uptake in this assay: PRO1265, PRO1283, PRO1279, PRO1303, PRO1306, PRO1325, PRO1565 and PRO1567.

The following PRO polypeptides tested positive as inhibitors of glucose and/or FFA uptake in this assay: PRO1194, PRO1190, PRO1326, PRO1343, PRO1480, PRO1474, PRO1575 and PRO1760.

**EXAMPLE 150: Chondrocyte Re-differentiation Assay (Assay 110)**

This assay shows that certain polypeptides of the invention act to induce redifferentiation of chondrocytes, therefore, are expected to be useful for the treatment of various bone and/or cartilage disorders such as, for example, sports injuries and arthritis. The assay is performed as follows. Porcine chondrocytes are isolated by overnight collagenase digestion of articular cartilage of metacarpophalangeal joints of 4-6 month old female pigs. The isolated cells are then seeded at 25,000 cells/cm<sup>2</sup> in Ham F-12 containing 10% FBS and 4 µg/ml gentamycin. The culture media is changed every third day and the cells are then seeded in 96 well plates at 5,000 cells/well in 100 µl of the same media without serum and 100 µl of the test PRO polypeptide, 5 nM staurosporin (positive control) or medium alone (negative control) is added to give a final volume of 200 µl/well. After 5 days of incubation at 37°C, a picture of each well is taken and the differentiation state of the chondrocytes is determined. A positive result in the assay occurs when the redifferentiation of the chondrocytes is determined to be more similar to the positive control than the negative control.

The following polypeptide tested positive in this assay: PRO1265, PRO1250, PRO1430, PRO1356, PRO1275, PRO1274, PRO1286, PRO1273, PRO1283, PRO1279, PRO1306, PRO1325, PRO1343, PRO1418, PRO1565, PRO1474, PRO1787, PRO1556 and PRO1801.

**EXAMPLE 151: Induction of Pancreatic β-Cell Precursor Proliferation (Assay 117)**

This assay shows that certain polypeptides of the invention act to induce an increase in the number of pancreatic β-cell precursor cells and, therefore, are useful for treating various insulin deficient states in mammals, including diabetes mellitus. The assay is performed as follows. The assay uses a primary culture of mouse fetal pancreatic cells and the primary readout is an alteration in the expression of markers that represent